VKM
Vitenskapskomiteen for mat og miljø
Norwegian Scientific Committee for Food and Environment

VKM Protocol

Protocol for a benefit and risk assessment of potassium chloride as salt replacer

From the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food and Environment

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22.06.2021

ISBN: 978-82-8259-366-3
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Cover photo: pxhere.com

Suggested citation: VKM, Tor A Strand, Knut Tomas Dalen, Kristin Holvik, Inger Therese L Lillegaard, Vegard Lysne, Martinus Løvik, Bente Mangschou, Christine L Parr, Lisbeth Dahl, Anine C Medin, Catherine Schwinger, Tonje H Stea, Lene Frost Andersen (2021). Protocol for a benefit and risk assessment of potassium chloride as salt replacer. Protocol from the Panel on Nutrition, Dietetic Products, Novel Food and Allergy of the Norwegian Scientific Committee for Food and Environment. ISBN: 978-82-8259-366-3, ISSN: 2535-4019. Norwegian Scientific Committee for Food and Environment (VKM), Oslo, Norway.

Protocol for a benefit and risk assessment of potassium chloride as salt replacer

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The protocol has been assessed and approved by the Panel on Nutrition, Dietetic Products, Novel Food and Allergy. Members that contributed to the assessment and approval of the protocol in addition to Tor A Strand, Knut Tomas Dalen, Kristin Holvik, Vegard Lysne and Martinus Løvik (in alphabetic order):

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Competence of VKM experts

Persons working for VKM, either as appointed members of the Committee or as external experts, do this by virtue of their scientific expertise, not as representatives for their employers or third-party interests. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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Abbreviations and acronyms

AHRQ – Agency for Healthcare Research and Quality, US
AMSTAR – A MeaSurement Tool to Assess systematic Reviews
COT – The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, UK
DRI – dietary reference intake
DRV – dietary reference value
EFSA – European Food Safety Authority
GRADE – Grading of Recommendations Assessment, Development and Evaluation
KBS – nutritional calculation software (KostBeregningsSystem)
KCl – potassium chloride
NaCl – sodium chloride
NCD – non-communicable disease
NASEM – National Academies of Sciences, Engineering, and Medicine
NutriGRADE – A Scoring System to Assess and Judge the Meta-Evidence of Randomized Controlled Trials and Cohort Studies in Nutrition Research
PICO – Population, Intervention, Comparison and Outcome
PROSPERO – The International Prospective Register of Systematic Reviews
RCT – randomised controlled trial
SACN – Scientific Advisory Committee on Nutrition (UK)
SLR – systematic literature review
UL – tolerable upper intake level
VKM – Vitenskapskomiteen for mat og miljø (Norwegian Scientific Committee for Food and Environment)
WHO – World Health Organization

1 The request from the Norwegian Directorate of Health

1.1 Background

Norway has committed to the World Health Organization's (WHO) Global Action Plan for the Prevention and Control of NCDs (2013-2020) and the target of a 25% reduction in premature mortality from non-communicable diseases (NCDs) (WHO, 2013). One of the goals of the WHO Action Plan is a 30% reduction in salt (sodium chloride, NaCl) intake by 2025. According to WHO, reducing salt intake has been identified as one of the most cost-effective dietary measures for NCD reduction (WHO, 2017). High sodium intake and insufficient intake of potassium can cause high blood pressure, which increases the risk of cardiovascular diseases (WHO, 2020). Updated dietary reference intakes for sodium and potassium from the US and Canada that is relevant for Norway, were issued in 2019 (National Academies of Sciences and Medicine, 2019). In addition, the European Food Safety Authority (EFSA) published dietary reference values for sodium in September 2019 (EFSA, 2019).

The Norwegian Directorate of Health's Action Plan on Salt Reduction 2014-18 set a target of a 15% reduction in salt intake by 2018 and a 30% reduction by 2025 (Helsedirektoratet, 2019b). In Norway, the mean population intake of salt is estimated to be approximately 10 grams/day in men, and somewhat less in women. The estimates include salt present in food and beverages as well as the discretionary salt added during cooking and eating. The estimates are supported by the findings of the population-based Tromsø Study 2015–2016. Based on an analysis of 24-hour urine samples from around 500 participants (age 40–69 years), the daily salt intake was estimated to be 10.4 grams in men and 7.6 grams in women (Meyer et al., 2019). The long-term target is 5 grams of salt/day (Helsedirektoratet, 2015). The Salt Partnership established in Norway in 2015 by enterprises in the food industry and the food retail, the hotel, restaurant and catering industry, trade organisations and associations, research groups, interest groups, and health authorities have set corresponding targets (Helsedirektoratet, 2019b). The Salt Partnership constitutes Action Area 1 in the letter of intent (Memorandum of Understanding) between the Norwegian health authorities and the food industry for facilitating a healthier diet in the population, which targets a reduction in mean population intake of salt to 8 g/day by 2021, and to 7 g/day by 2025 (Helsedirektoratet, 2019a). This corresponds to a 20 and 30% reduction in population intake of salt, respectively. Within the Salt Partnership, the food industry is working systematically and in line with common objectives to reduce the level of salt in its foods. In Norway, 'salt lists' were compiled showing the recommended salt content targets for 100 food categories in 2018. A 2018 survey of progress on target achievement indicated, among other things, that the average salt content was on or below the salt target in 40 percent of the main categories, while the weighted average was on or below the salt target in 60 percent of the main categories (Helsedirektoratet, 2019c).

Salt has several functions in food: it adds flavour, preserves food and inhibits the growth of some pathogenic microorganisms, increases water-binding to proteins in meat and fish, and has a technological function in bread and cheese production. Around 70-80% of dietary salt derives from industrially produced (processed) foods (Norge, 2020). Unprocessed foods account for only 10% of sodium intake. Discretionary addition of salt to food during cooking and eating contributes to the remaining overall dietary salt intake (SINTEF, 2012).

A reduction of salt in processed food is thus an important measure in reducing population salt intake. One possible strategy is to use salt replacers to reduce the sodium content in food. The objective of the Norwegian SALTO research project was to reduce the content of sodium in a range of foods (SINTEF, 2012). Among other things, the project assessed relevant salt replacers for use in industrial food production (SINTEF, 2014). A partial replacement of NaCl by potassium chloride (KCl) has proven to be a viable option for sodium reduction in terms of product flavour, shelf-life, and technological properties.

In 2014, the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen for mattrygghet, VKM) published the report "Benefit and risk assessment of increasing potassium by replacement of sodium chloride with potassium chloride in industrial food production" (VKM, 2014). In the report, VKM estimated population health effects of increasing the amount of KCl in foods at the expense of NaCl. The scenarios requested in the task commissioned by the Norwegian Food Safety Authority were for replacement of NaCl by KCl at by-weight ratios of 30:70, 50:50, 70:30. VKM concluded that the proportion of people at increased risk of adverse health effects from an increase in potassium in processed foods is far greater than the proportion of people likely to benefit from the increase in potassium. VKM did not assess the population health outcomes of a corresponding reduction in NaCl, as this was not part of the commission. Further, VKM concluded that if NaCl is replaced, partially or fully, by KCl at the same molarity, then the microbiological risk would remain the same irrespective of food group.

In 2017, the British authorities, represented by the Scientific Advisory Committee on Nutrition (SACN) in collaboration with the Committee on Toxicity (COT) published a joint benefit-risk assessment of replacing 15-25% of sodium in foods with potassium (calculated on a per-mole basis) (SACN/COT, 2017). The report was based on independent assessments from SACN (SACN, 2017) and COT (COT, 2017). A 15-25% substitution of NaCl by KCl on a per-mole basis corresponds to a weight-basis substitution of approximately 19-30%. SACN and COT jointly concluded that the potential benefits of using potassium-based salt replacers to reduce sodium in foods outweigh the potential harm at a population level. The SACN/COT report indicates that approximately 1% of the population might potentially be at risk of hyperkalemia from increased use of KCl in place of NaCl. At the same time, SACN found that a somewhat higher potassium intake would benefit a healthy population, as this is conducive to lowering blood pressure and to reduce the risk of stroke. The Norwegian Directorate of

Health has consulted with the National Nutrition Council, which finds that the conclusions of the SACN/COT report are well-founded, and that a new assessment should be undertaken in Norway, based on the UK report. The National Nutrition Council suggested for the Norwegian Directorate of Health to commission a benefit-risk assessment from VKM on substitution of sodium by potassium that would also include beneficial health outcomes of sodium reduction in an assessment based on diet in Norway.

Norwegian food industry, represented by the SaltNett network within the Norwegian Salt Partnership, has called for a more explicit recommendation from the authorities regarding the scope for using potassium as a salt replacer in food. In a memorandum addressed to the Norwegian Directorate of Health of April 2018, SaltNett pointed out that international studies and company trials have demonstrated that replacing NaCl by KCl by up to 20-30% is for most foods an upper limit as regard to flavour (see Appendix *Memorandum Overall assessment of the use of potassium chloride as a salt replacer in foods).* This means that the scenarios employed in the UK will also apply to the Norwegian situation.

1.2 Terms of reference

The Norwegian Directorate of Health commissions VKM to carry out a benefit-risk assessment of potassium chloride as a salt replacer in the production of foods, taking into account the health outcomes of increased potassium and corresponding reduced sodium intake in the population from children age 12 months upwards. According to the Norwegian food industry, replacing up to 20-30% of NaCl with KCl on a weight basis is realistic.

- What will the dietary intake of sodium and potassium be if 0-30% of added NaCl is replaced by KCl?

- What are the potential health outcomes for the population of a reduced intake of sodium chloride and a correspondingly increased intake of potassium chloride?
    - Assess the health outcomes of reduced intake of sodium and increased intake of potassium.

Are there any particularly vulnerable groups in the population as regards increased intake of potassium or reduced intake of sodium based on this scenario? Vulnerable groups should be described.

2 Aim, objectives and research questions

The overall aim is to assess the benefits and risks related to reduced intake of salt (NaCl) and correspondingly increased intake of potassium (K) when using KCl as salt replacer in the Norwegian population.

The objectives:

• Identify and characterise health effects for different age groups related to 0-30% reduced intake of added NaCl combined with correspondingly 0-30% increased intake of K from salt replacers.

- Identify established health-based guidance values for K and Na
- If possible, identify or describe the point of departure for health benefits related to reduced NaCl and benefits and risks related to correspondingly increased KCl
- Identify vulnerable groups with health conditions that may be negatively affected by increased supplemental K
- Describe uncertainty and data gaps related to the health effects

• Estimate the exposure

- Estimate exposure of Na and K when 0-30% of NaCl is replaced by KCl for different age groups
- Identify population groups at risk of low and high K intakes
- Identify population groups at risk of low and high Na intakes
- Describe uncertainty and data gaps related to the exposure estimates

• Assess health risks associated with exposure to reduced Na combined with correspondingly increased K, based on exposure and potential health risks identified, and describe uncertainty that may have an impact on the conclusions

• Identify and describe main knowledge gaps that may have an impact on the conclusions

2.1 Target population

Norwegian population ≥ 1year of age.

Additionally, we will identify and describe population groups that may be vulnerable to increased intakes of K or reduced intakes of Na from salt replacers (0-30% exchange). We will identify these population groups from previous reports fro m (EFSA, 2019; National Academies of Sciences and Medicine, 2019; SACN/COT, 2017; VKM, 2014; VKM, 2017) in addition to the systematic literature reviews (SLRs) and meta-analyses identified in our literature search described in section 4.2.

2.2 Limitations

The health effects of reduced sodium intake are well established and a basis for the WHO Action Plan. Therefore, we will not identify health effects of reduced Na alone, only combined with increased K intakes. For health effects from reduced Na we refer to (WHO, 2012; WHO, 2013; WHO, 2016).

This assessment relates to supplemental K as Na replacer, and not increased naturally occurring K in the diet (e.g. from increased intake of fruits and vegetables).

3 General methodology for benefit and risk assessment

The benefit and risk assessment of potassium chloride as salt replacer will follow the first steps in BRAFO tiered approach (Hoekstra et al., 2012) when relevant. In the EFSA guidance, "a stepwise approach is recommended for the risk-benefit assessment, i.e. i) initial assessment, addressing the question of whether the health risks clearly outweigh the health benefits or vice versa, ii) refined assessment, aiming at providing semi-quantitative or quantitative estimates of risks and benefits at relevant exposure by using common metrics, and iii) comparison of risks and benefits using a composite metric such as DALYs or QALYs to express the outcome of the risk-benefit assessment as a single net health impact value. The outcome of each step of the assessment should also include a narrative of the strengths and weaknesses of the evidence base and its associated uncertainties. After each step of the risk-benefit assessment, discussion should take place between the risk-benefit assessor and the risk-benefit manager on whether sufficient information has been provided or whether the terms of reference should be refined in order to proceed with the next step of the assessment."

4 Health effects – benefit and hazard identification and characterisation

To evaluate the benefits and risks related to reduced intake of NaCl we will base our work on previous WHO reports. To evaluate the health effects of reduced Na intake and a corresponding increase in K intake from the use of KCl as Na replacer we will base our work on relevant previous reports and an updated literature search.

4.1 Previous reports

We have identified the following reports as relevant for our work:

Two VKM opinions on potassium (VKM, 2014; VKM, 2017); evaluating potassium chloride as salt replacers (2014) and maximum levels of potassium in food supplements (2017).

Three statements on health effects related to potassium-based sodium replacers from Scientific Advisory Committee on Nutrition (SACN) and Committee on Toxicology (COT) in the UK from 2017 (COT, 2017; SACN, 2017; SACN/COT, 2017).

The EFSA opinion from 2019 on establishing dietary reference values (DRVs) for potassium from (EFSA, 2019).

A systematic review by the Agency for Healthcare Research and Quality (AHRQ), US from 2018 regarding the effects of Na reduction and increased K intake on blood pressure and risk for cardiovascular diseases (CVD) and renal disease outcomes and related risk factors (Newberry et al., 2018).

A systematic approach to establishing dietary reference intakes (DRIs) for sodium and potassium from National Academies of Sciences, Engineering, and Medicine (NASEM) from 2019, US (National Academies of Sciences and Medicine, 2019).

Three reports from WHO evaluating health effects related to reduced Na (WHO, 2012; WHO, 2013; WHO, 2016).

In August 2021, we became aware that WHO are currently preparing Guidelines for low-sodium salt replacers. We also became aware of an ongoing Cochrane Systematic Review and meta-analysis investigating health effects related to salt replacers, including health outcomes related to increased potassium, such as hyperkalemia. The Cochrane systematic review will most likely be available by the end of 2021 (personal communication Dr Yamamota and Dr Nishida, WHO Nutrition Policy and Scientific Advice Unit, 24. August 2021). Upon receiving this information, we decided to use the results from this Cochrane systematic review in our benefit and risk assessment.

4.2 Literature search - data selection and methodology

4.2.1 Systematic literature search and selection

A first systematic literature review has been conducted to identify published systematic reviews and meta-analyses and primary studies limited to RCTs, on potassium or salt/sodium replacers. The main aim of our search is to identify systematic reviews and meta-analyses or recent RCTs on health benefits and risks related to a reduced intake of NaCl combined with an increased intake of K when KCl is used as Na replacement. Good quality literature that fulfills the inclusion criteria will be evaluated with special focus on comparison to findings and conclusions in previous reports relevant for our assignment. Any conflicts with previous reports will be evaluated systematically with quality assessment of the papers and an evaluation of the evidence.

To identify relevant literature for our terms of reference, we formulated the following PICO question: "What are the health effects in the population ≥1 year, including specific patient groups, of increased potassium intake from salt substitutes. Health effects from reduced sodium chloride intake by substitution with potassium chloride should be included." The literature search was based on the PICO frame in Table 4.2.1-1.

Table 4.2.1-1. PICO frame for the systematic literature search.

Population	Intervention	Comparison	Outcome
General population including children, patients with reduced kidney function, CHD/CVD, diabetes, hypertension and obesity	Potassium, potassium chloride, salt replace*, sodium replace*	No increase in the intake of potassium from current levels.	Stroke, blood pressure/ hypotension/ hypertension hyperpotassemia, kidney function, renal failure, CHD/CVD, cardiac arrest, arrythmia, diabetes

Literature searches have been performed in MEDLINE, Embase, Cochrane, and Epistemonikos (covering the period from 2018) and in PROSPERO (covering the period from 2011) to identify new studies not included in the previous reports. The results from the searches will be screened, as described below, in the summer 2021. Updated and/or additional searches may be performed later if needed, and papers may also be included via "snowballing"/citation chasing.

To identify search terms and text words for the relevant health outcomes, VKM used previous reports listed above and the Panel's expertise. A systematic approach will be used for the selection of papers/studies from the literature search. Screening of titles and abstracts will be performed in a pairwise blinded manner using Rayyan, a web application for systematic reviews (Ouzzani et al., 2016). The screening will be performed against predefined inclusion/exclusion criteria. These criteria are given in Table 4.2.1-2 below. After the first round of screening, the blinding will be removed, and the reviewers discuss conflicting decisions. If the two reviewers are unable to reach an agreement, the paper in question will be included.

The potentially relevant papers selected via the screening procedure based on title and abstract will then be reviewed in full text. This will be done in a similar, pairwise blinded manner, using Rayyan, and based on the same inclusion and exclusion criteria. Full-text papers will be quality assessed as described below (4.2.2 Methodology for quality assessment).

Our PICO frame and literature search strategy were somewhat different than the strategies described in the above-mentioned upcoming Cochrane systematic review. We will therefore include results from our own literature review in the benefit and risk assessment in addition to results from the Cochrane systematic review and WHO guidelines.

Detailed search strategy is given in Appendix I.

Table 4.2.1-2. Inclusion and exclusion criteria for literature selection of systematic reviews, meta-analyses and RCTs.

Criteria for inclusion	Systematic reviews and meta-analyses of RCTs and original RCTs investigating positive or negative health effects from supplemental potassium Systematic reviews, meta-analyses and RCTs investigating positive or negative health effects from replacement of sodium (chloride) with potassium (chloride) – so called salt replacers Systematic reviews, meta-analyses and RCTs investigating the general population (age ≥ 1 years). Studies in certain patient groups, such as those with type 2 diabetes, CHD/CVD, hypertension, reduced kidney function, obesity and muscular skeleton diseases will be evaluated for inclusion. Systematic reviews, meta-analyses and RCTs investigating the following outcomes -hypotension/ low blood pressure -hypertension/ high blood pressure - cardiovascular disease - cardiac arrest - renal failure - reduced kidney function - diabetes type 2 - mortality Publication registered in an appropriate database such as PROSPERO (SLR/meta-analyses) or clinicaltrials.gov (RCTs)
Criteria for exclusion	Systematic reviews, meta-analyses and RCTs investigating positive or negative health effects from increased dietary potassium Systematic reviews and meta-analyses including only human observational studies or animal studies Systematic reviews, meta-analyses and RCTs investigating age groups ≤ 1 years Systematic reviews, meta-analyses and RCTs investigating the effect of reduced sodium alone – without potassium

4.2.2 Methodology for quality assessment

For reviews of systematic reviews (umbrella reviews), individual systematic reviews or meta-analyses, we will use the grading conducted by the authors when available if the instrument used is considered reliable, e.g., GRADE or NutriGrade.

We will use Amstar 2 to assess the quality of included systematic reviews and meta-analyses.

We will use appropriate tools to assess the quality of the included RCTs.

When we have identified and quality assessed all systematic reviews, meta-analyses, and RCTs from our literature search, we will evaluate new papers with relevant information that can substantially alter the conclusions of the previous reports from the SACN/COT statements (2017), Newberry et al. (2018) or NASEM report (2019) and that were not included in those statements/reports.

If the identified SLR/meta-analyses and RCTs from our literature search do not support the conclusions from the SACN or NASEM reports, we will use the literature from our search and from these reports to update the weight of evidence.

5 Exposure assessment

For the benefit assessment of reduced Na and concurrent increased K intakes, we will estimate the habitual daily exposure to Na and K.

Furthermore, we will estimate scenarios for the daily exposure to total Na and K if 0-30% of added NaCl is substituted with KCl.

The exposure estimation will be semi-deterministic using the observed individual means method, and if suitable also with the use of probabilistic methods

The mean, median, and the 5th and 95th percentiles, will be presented for the exposure calculations.

For the risk assessment of high K intakes, the focus for the exposure estimates will be salt replacement (0-30% scenarios) and supplemental K from food supplements, and fortified foods in general.

Exposures to Na and K will be estimated based on dietary intakes from the National dietary surveys "Spedkost", "Småbarnskost 3", "Ungkost 3", and "Norkost 3" covering the age groups 1-70 years. Other Norwegian dietary surveys can be used as supplementary background information for intake of Na and K.

The nutritional calculation software KBS contains nutrient values for Na and K. NaCl intakes are, however, difficult to estimate from dietary surveys. There is also a lack of knowledge about consumption of household salt in the Norwegian population. The best method for measuring habitual Na intake is by measuring Na excretion from several 24-hour urine collections in the same person.

The most recent Na data from Norway are based on a single 24-hour urine collection in the seventh wave of the Tromsø study (Tromsø 7), carried out in 2015-16 (www.tromsostudy.com). One 24-hour urine collection was obtained from 496 participants in Tromsø 7 aged 40-69 years and analysed for Na, K, creatinine, and iodine (Meyer et al., 2019). We will use these biomonitoring data to evaluate the estimated Na and K intake from the national dietary surveys.

Biomonitoring-data on Na and K in Norwegian children or adolescents is, to our knowledge, lacking.

Person-specific body weights will be used when available, otherwise, study and gender-specific body weights will be used.

6 Benefit and risk characterisation

The benefit and risk characterisation will be based on the estimated exposures (chapter 5) of salt, and the replacement scenarios of Na with K and K doses not to give rise to safety concerns (chapter 4), and benefits from reduced Na from K based salt replacers.

The benefit and risk assessment in this chapter will be restricted to describing the benefits and risks from replacing NaCl by KCl. The outcomes will be restricted to known benefits from decreased NaCl and increased KCl, and known risks related to increased KCl, including vulnerable groups to high potassium intakes, such as persons with impaired kidney function.

7 Uncertainty and data gaps

Factors introducing uncertainty in the various steps of the assessments and data gaps will be identified and described.

8 References

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Appendix I

Search strategy for literature search

Database: **Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) 1946 to June 02, 2021**
Dato: 03.06.2021
Antall treff: 2533

#	Searches	Results
1	Potassium Chloride/	17947
2	Potassium/	101862
3	potassium.tw,kf.	146440
4	((sodium or sodium chloride or salt or natrium) adj2 (replac* or substitut*)).tw,kf.	1750
5	("sodium chloride" adj2 (replac* or substitut*)).tw,kf.	176
6	or/1-5	217641
7	(2018* or 2019* or 2020* or 2021*).ed,ep,yr,dp,dt.	5631783
8	6 and 7	22222
9	limit 8 to (danish or english or interlingua or multilingual or norwegian or swedish)	21658

#	Searches	Results
10	Animals/ not (animals/ and humans/)	4803318
11	9 not 10	18354
12	limit 11 to "therapy (maximizes specificity)"	398
13	("randomized controlled trial" or "controlled clinical trial").pt. or (randomized or randomised or randomly or rct or placebo or trial or groups).tw,kf,bt.	3286128
14	12 or (11 and 13)	2533

Database: **Embase 1974 to 2021 June 02**
Dato: 03.06.2021
Antall treff: 3582

#	Searches	Results
1	potassium chloride/	28113
2	potassium intake/	2599
3	high potassium intake/	241
4	potassium/	102244

#	Searches	Results
5	potassium.tw,kw.	171021
6	((sodium or sodiumchloride or salt or natrium) adj2 (replac* or substitut*)).tw,kw.	1944
7	("sodium chloride" adj2 (replac* or substitut*)).tw,kw.	171
8	or/1-7	243814
9	(2018* or 2019* or 2020* or 2021*).yr,dd,dp,dc.	6496310
10	8 and 9	35166
11	limit 10 to (english or norwegian or polyglot or swedish)	34418
12	limit 11 to (embase or conference abstracts)	28431
13	(animal/ or exp nonhuman/ or Animal experiment/) not ((animal/ or exp nonhuman/ or Animal experiment/) and exp human/)	6220636
14	12 not 13	20293
15	limit 14 to "therapy (maximizes specificity)"	668
16	limit 14 to (randomized controlled trial or controlled clinical trial)	982

#	Searches	Results
17	(randomized or randomised or randomly or rct or placebo or trial or groups).tw,kw.	4404608
18	15 or 16 or (14 and 17)	3582

Database: Cochrane Database of Systematic Reviews: Issue 6 of 12, June 2021; Cochrane Central Register of Controlled Trials: Issue 5 of 12, May 2021
Dato: 03.06.2021
Antall treff: 3352

ID	Search	Hits
#1	[mh ^"Potassium Chloride"]	328
#2	[mh ^Potassium]	2208
#3	potassium:ti,ab	9041
#4	((sodium or "sodium chloride" or sodiumchloride or salt or natrium) NEAR/2 (replac* or substitut*)):ti,ab	139
#5	{or #1-#4}	10057
#6	#5 with Cochrane Library publication date Between Jan 2018 and Dec 2021	3365
#7	#6 in Trials	3352

Database: Epistemonikos

Dato: 03.06.2021

Antall treff: 17 (Primary study)
Kommentar: Begrensninger i databasens søkemuligheter gjør det nødvendig med et forenklet søk.

title/abstract: (sodium or "sodium chloride" or sodiumchloride or salt or natrium) and (replac* or substitut*) **2018-2021**

Database: **PROSPERO**
Dato: 16.06.2021
Antall treff: 178 treff (140 etter dublettsjekk i EndNote)

MeSH DESCRIPTOR Potassium Chloride: 1 treff

MeSH DESCRIPTOR Potassium: 26 treff

potassium: 117 treff (i "intervention")

(sodium AND replac*): 12 treff (i "intervention")

(sodium AND substitut*): 8 treff (i "intervention")

(salt AND replac*): 4 treff (i "intervention")

(salt AND substitut*): 10 treff (i "intervention")